continuous detection of said cleavage reaction by monitoring change in fluorescent intensity.

Claim 103: This claim finds support in the paragraph bridging pages 15 and 16.

Claim 104: This claim finds support in the paragraph bridging pages 15 and 16.

Claim 105: This claim finds support at page 15, lines 20 to 23.

Claim 106: This claim finds support in original Claim 12 et seq.

Claim 107: This claim finds support in original Claim 14 et seq.

Claim 108: This claim finds support at page 10, lines 9 to 12, et seq.

(1) Patent

In accordance with 37 C.F.R. §1.607, Applicants seek to provoke an Interference with U.S. Patent 5,538,848, issued July 23, 1996.

(2) The proposed Count to define the Interference is set forth below.

> A method for continuously detecting a cleavage reaction by a fluorometric assay, which method includes the following steps:
>
> (i) producing a double stranded nucleic acid sequence that comprises at least one fluorescent donor and acceptor pair, wherein said fluorescent donor and acceptor are positioned on said double stranded nucleic acid sequence such that fluorescence is quenched by the transfer of donor fluorescence to the acceptor;
>
> (ii) contacting said double stranded nucleic acid sequence with an enzyme that catalyzes a cleavage reaction which results in the separation of said donor and acceptor pair; and

(iii) continuously monitoring the change in fluorescence intensity as said cleavage reaction proceeds.

or

A method for monitoring nucleic acid amplification comprising:

performing nucleic acid amplification on a target polynucleotide using a nucleic acid polymerase having 5'-3' nuclease activity, a primer capable of hybridizing to said target polynucleotide, and an oligonucleotide probe capable of hybridizing to said target polynucleotide, 3' relative to said primer,

said oligonucleotide probe existing in at least one single-stranded conformation when unhybridized where said quencher molecule quenches the fluorescence of said reporter molecule, said oligonucleotide probe existing in at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched, the fluorescence intensity of said reporter molecule being greater than the fluorescence intensity of said quencher molecule when said probe is hybridized to said target; polynucleotide,

said nucleic acid polymerase digesting said oligonucleotide probe during amplification to separate said reported molecule from said quencher molecule; and

monitoring the fluorescence of said reporter molecule, the generation of fluorescence corresponding to the occurrence of nucleic acid amplification.

(3) Identification of at Least One Claim in Patent Corresponding to Proposed Count

At least Claim 1 of the '848 Patent corresponds to the proposed Count. In fact, this claim is identical to one alternative of the proposed Count.

(4) Presentation of At Least One Claim Corresponding to the Count

Applicants note that at least Claim 102 corresponds to the proposed Count.

(5) Application of Terms of Application Claim (s) Corresponding to the Count Not Contained in the Original Filed Patent Application

Support for current pending Claims 67 through 100 in the disclosure is as follows:

Claims 64 and 65 find support in original Claim 1, and at page 12, lines 13-15.

Claim 66 finds support in original Claims 1, 12, 13 and 14.

Claim 67 finds support in original Claims 1 and 3, page 15, lines 11 to 26 (discloses donor/acceptor fluorescent pair), page 10, line 25 to page 11, line 14, wherein the preferred use of linker arms to effect attachment of such fluorophores is provided, and page 34, line 16 to page 35, line 17, wherein the effects of such linker arms on quenching (inhibition) are discussed.

Claims 68 and 69 find support in Example 3.

Claims 70 and 71 find support in original Claim 14.

Claim 72 finds support in Example 2.

Claim 73 finds support in Examples 2 and 3.

Claim 74 finds support in Example 2.

Claim 75 finds support, e.g., in Example 2, page 35, lines 3-6.

Claim 76 finds support, e.g., in Example 2, page 35, lines 10-12.

Claims 77 and 78 find support, e.g., at page 11, lines 5 to 9.

Claims 79 and 80 find support, e.g., at page 10, line 20 to page 11, line 9, and the paragraph bridging pages 34 and 35.

Claim 81 finds support in original Claim 3.

Claim 82 finds support at page 12, lines 16 to 21.

Claim 83 finds support at page 15, last paragraph.

Claims 84, 85, 86, 87, 88 and 80 find support at page 10, lines 9 and 10.

Claims 90 and 91 find support at page 11, lines 9 to 14, wherein the use of linker arms is described, as well as page 34, line 15 to page 35, line 17.

Claims 92 through 101 find support is the disclosure as set forth above for Claims 66, 67, 69 through 76, and 80, respectively. [92 (66, 67); 93 (64); 94 (70); 95(71); 96 (72); 97 (73); 98 (74); 99 (75); 100 (76); 101 (80)]

Support for newly-submitted Claims 102 through 108 is discussed above.

(6) Requirements of 35 U.S.C. §135(b) are Met

35 U.S.C. §135(b) requires that. for Applicants seeking to provoke an Interference with a patent, a claim be submitted which is directed to the same or substantially the same patentable subject matter at least one year prior to the issue date of the patent for which an Interference is sought. This requirement is satisfied as the present application,

submitted on December 30, 1994, contained claims directed to substantially the same subject matter as is being pursued herein, which the Examiner has suggested is not patentable over the '848 patent claims. For example, original Claim 1 was broadly directed to a method for detecting an enzyme-mediated nucleic acid cleavage reaction based on change (increase in fluorescence).

Also, original Claims 12 and 14 respectively provided for said cleavage reaction to be effected during nucleic acid amplification, and specifically polymerase chain reaction. Therefore, Applicants had presented a claim prior to the issue date of the '848 patent that is directed to the same or substantially the same subject matter as that of the conflicting patent with which an Interference is now sought.

(7) Requirements of 37 C.F.R. §1.608(a) are Satisfied

The Livak patent has an apparent effective filing date of November 16, 1994. The effective filing date of this application is December 30, 1994. As the effective filing date of this application is less than three months prior to the effective filing date of the '848 patent, no §608(b) showing is required as Applicants respectfully submit that there is a basis upon which Applicants are entitled to a judgment relative to the Patentee.

Therefore, based on the foregoing, all of the requirements for provoking an Interference between this application and the '848 patent are met.

Turning now to the Office Action, Applicants respectfully note that all of the prior art rejections were based on the Livak patent. In order to overcome this rejection,

Applicants previously submitted a §131 Declaration. However, this was not accepted on the basis that Applicants were pursuing claims that were not patentably distinct from those in the Livak patent.

Applicants respectfully note that the Livak patent has an effective filing date of November 16, 1994, which is less than three months prior to the effective filing date of this application (December 30, 1994). As the effective filing date of this application is less than three months prior to the effective filing date of the Livak patent, in accordance with §608(b), no §608(a) Declaration is required to antedate the Livak patent because Applicants respectfully aver that there is a reasonable basis for concluding that Applicants will prevail in an Interference with the Livak patent. This statement, in accordance with to 37 C.F.R. §1.608(b), should overcome the outstanding prior art rejections.

Also, new Claims 102 through 108 should be patentable for substantially the same reasons. Essentially, no prior art reference or references known to Applicants suggest the concept of continuously detecting a cleavage reaction, that involves cleavage of a double stranded nucleic acid sequence, which comprises a donor/acceptor pair that is quenched in the uncleaved state, and which becomes unquenched upon cleavage resulting in an increase in fluorescence intensity, that allows for the cleavage reaction to be continuously detected.

As discussed in the application, the advantages of the subject fluorescent assay are unparalleled in relation to previous fluorimetric assays. For example, the subject methods

allow for almost immediate detection of target nucleic acid sequences, continuity of reaction monitoring, sensitivity, specificity, and capacity for automation, e.g., through 96-well fluorescence microplate readers.

Based on the foregoing, Applicants respectfully request that an Interference be declared between this application and the '848 patent.

Respectfully submitted,

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